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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/046,833	03/24/1998	DAKAI LIU	ENZ-56(DIV4)	2594

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EXAMINER	
GUZO, DAVID	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 06/26/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N . 09046833	Applicant(s) DAKAI, ET AL,
	Examiner David Guzo	Art Unit 1636

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 March 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *75-90* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *75-90* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 75-82, 88-89 and 90 are rejected under 35 U.S.C. 102(e) as being anticipated by Finer et al. or Bodner et al.

Applicants, Finer et al. (U.S. Patent 5,686,279, issued 11/11/97, see whole document, particularly Columns 10-11, 17, Claims 1-11) and Bodner et al. (U.S.Patent 5,681,746, issued 10/28/97, see whole document, particularly Columns 11-22) all recite packaging cell lines for propagating retroviral vectors independent of helper viruses, said viral vectors comprising a nucleic acid component and two different non-nucleic acid components wherein said two different non-nucleic acid components can be two different envelope proteins (one having a tropism for the packaging cell (which can be a murine cell) and one having a tropism for a different target cell (which can be from a different species, i.e. human, and can be a epithelial cell or marrow cell or T-cell, etc.),

said nucleic acid and non-nucleic acid components being capable of forming a complex (i.e. a viral particle) and wherein said nucleic acid sequences encoding said components can be stably integrated into the cell genome or can be present extra chromosomally. The nucleic acid component of the vector can comprise sequences from two viruses that are native to the cell (i.e. encoding sequences for two different ecotropic or amphotropic envelopes, etc.). Therefore, Finer et al. and Bodner et al. teach the claimed invention.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 83, 85 rejected under 35 U.S.C. 103(a) as being unpatentable over Finer et al. or Bodner et al., either in view of Respess et al.

Applicants claim a packaging cell comprising a viral vector which encodes an antisense RNA targeted against a mRNA coding for an undesirable protein in a target cell.

Finer et al. and Bodner et al. are cited as in the above 35 USC 102(e) rejection of claims 75-82 and 88-90. Neither Finer et al. nor Bodner et al. teach expression of antisense sequences by viral vectors.

Respess et al. (U. S. Patent 6,013,517, issued 1/11/00, effective filing date 5/9/94, see whole document, particularly Columns 14-15, Claims 1, 8 and 11) recites the generation of packaging cell lines capable of generating retroviral vectors which are capable of expressing antisense RNAs complementary to undesirable mRNAs (i.e. mRNAs coding for cellular proteins required for cell growth in cancer cells) produced by target cells.

The ordinary skilled artisan, seeking to generate retroviral vector packaging cells capable of generating retroviral vectors capable of expressing an antisense sequence directed against the mRNA from an undesirable gene in a target cell, would have been motivated to combine the teachings of Finer et al. or Bodner et al. on the generation of retroviral packaging cells with the characteristics of claims 75-82 and 88-90 with the teachings of Respess et al. on the packaging cells which generate retroviral vectors capable of expressing antisense sequences targeted against mRNAs from undesirable genes in target cells because the expression of antisense sequences targeted against

undesirable genes in target cells has been a well known techniques to inhibit the growth of undesirable target cells or inhibit virus replication, etc. It would have been obvious for the ordinary skilled artisan to do this because use of viral (retroviral) vectors to deliver antisense sequences to target cells, in the context of treatment of diseases, was well known in the art (see Respess et al.) and was a standard use of retroviral vectors. Given the teachings of the cited prior art and the level of skill of the ordinary skilled artisan at the time of applicants' invention, it must be considered that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claim 84 is rejected under 35 U.S.C. 103(a) as being unpatentable over Finer et al. or Bodner et al., either in view of Bujard et al.

Applicants claim a viral packaging cell line wherein the viral vector produced expresses a polypeptide of interest and an antisense RNA in a target cell.

Finer et al. and Bodner et al. are cited as in the above 35 USC 102(e) rejection. Neither Finer et al. nor Bodner et al. teach a packaging cell line producing a viral vector which expresses a polypeptide of interest and an antisense sequence in a target cell.

Bujard et al. (U.S. Patent 6,271,348, issued 8/7/01, effective filing date 6/7/95, see whole document, particularly Columns 18 and 21-22) recites the use of bi-directional promoters in viral vectors (which can be retroviral vectors) so that two gene products can be produced. The gene products can be two polypeptides of interest or two antisense sequences or a polypeptide and an antisense sequence.

The ordinary skilled artisan, seeking to generate a packaging cell line comprising a viral vector capable of expressing a polypeptide of interest and a antisense sequence in a target cell, would have been motivated to combine the teachings of Finer et al. or Bodner et al. with regard to the generation of packaging cell lines with the characteristics of claims 75-82 and 88-90 with the teachings of Bujard et al. on the use of viral vectors comprising bi-directional promoters for expression of multiple sequences encoding polypeptides and/or antisense sequences because the use of bi-directional promoters increases the versatility of viral vectors in that more than one sequence of interest can be expressed by a single vector. It would have been obvious for the ordinary skilled artisan to do this because being able to generate more versatile viral vectors capable of expressing two different sequences of interest would be desirable (See Bujard et al.). Given the teachings of the cited prior art and given the level of skill of the ordinary skilled artisan at the time of applicants' invention, it must be considered that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claims 83, 85, 86-87 are rejected under 35 U.S.C. 103(a) as being unpatentable over Finer et al. or Bodner et al., either in view of Dietz.

Applicants claim a packaging cell line comprising a viral vector which encodes an antisense RNA targeted against a mRNA coding fro an undesirable protein in a target cell and wherein the antisense RNA can be a part of a chimeric RNA molecule that comprises sequences from small nuclear RNAs (for example, U1 snRNA).

Finer et al. and Bodner et al. are cited as in the above 35 USC 102(e) rejection of claims 75-82 and 88-90. Neither Finer et al. nor Bodner et al. teach expression of antisense sequences by viral vectors.

Dietz (U.S. Patent 5,814,500, issued 9/29/98, filed 10/31/96, see whole document, particularly Columns 2-3, 8 and Claims 1-11) recites the use of retroviral vectors to express antisense sequences targeted against undesirable target genes and wherein the antisense RNA is part of a chimeric RNA molecule that comprises sequences from snRNAs (such as U1 snRNA).

The ordinary skilled artisan, seeking to develop packaging cell lines capable of generating retroviral vectors capable of expressing an antisense sequence or a chimeric antisense RNA molecule, would have been motivated to combine the teachings of Finer et al. or Bodner et al. on the generation of retroviral packaging cell lines with the characteristics of claims 75-82 and 88-90 with the teachings of Dietz concerning the use of retroviral vectors to express chimeric antisense sequences targeted against undesirable genes in target cells because the expression of antisense sequences targeted against undesirable genes was a well known technique in molecule biology and use of retroviral vectors to deliver chimeric RNAs to target cells was likewise known (Dietz). It would have been obvious for the ordinary skilled artisan to do this because delivery and expression of antisense sequences targeted against undesirable genes had been a well known (for almost two decades) technique in molecular biology. It would further have been obvious for the ordinary skilled artisan to select chimeric RNAs encoding antisense sequences and snRNAs because Dietz teaches that said chimeric

RNAs make superior delivery vehicles for delivering the antisense sequences to the target cells. Given the teachings of the cited prior art and the level of skill of the ordinary skilled artisan at the time of applicants' invention, it must be considered that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 88-90 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 88-90 are vague in the recitation of the phrase "virus that is native to" the cell line or target cell. It is unclear if this phrase means that the virus naturally infects and replicates within the cell or that the virus can infect the cell but not replicate in the cell, or that the virus genome is present in the cell but it is not replicated, etc.

No Claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Guzo whose telephone number is (703) 308-1906. The examiner can normally be reached on Monday-Thursday from 8:00 AM to 5:30 PM. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, can be reached on (703) 305-1998. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242. Faxes may be sent directly to the Examiner at (703) 746-5061.

Any inquiry of a general nature or relating to the status of this application or proceeding or relating to attachments to this Office Action should be directed to Patent Analyst Zeta Adams whose telephone number is (703) 305-3291.

David Guzo
June 20, 2002

DAVID GUZO
PRIMARY EXAMINER